

IN THE CLAIMS:

Claims 1-3, 6, 7, 10-15, 17-19, 21-23, 25, 26, 29, 31, 32, 35, 37-39, and 42 have been amended herein. Claims 4, 8, 9, 16, 20, 27, 28, 36, 40, 41, and 43-64 are cancelled herein. New claims 65-68 are presented herein. All of the pending claims are presented below. This listing of claims will replace all prior versions and listings of claims in the application. Please enter these claims as amended.

Listing of the Claims:

1. (Currently Amended) An isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species, said *thyA* mutant comprising:

~~a nucleic acid encoding an inactive *Lactococcus* thymidylate synthase gene and a gene encoding a heterologous prophylactic or therapeutic molecule;~~

wherein said strain of *Lactococcus* species comprises a thymidylate synthase gene comprising

at least 100 contiguous nucleotides that are at least 90% identical to ~~a region of~~ SEQ ID NO: 1; and

at least 100 contiguous nucleotides that are at least 90% identical to ~~a region of~~ SEQ ID NO: 2.

2. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 1, wherein said inactive *Lactococcus* thymidylate synthase gene has been inactivated by gene disruption.

3. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of any one of claim 1, 2, 5, or 6, wherein the *Lactococcus* species is *Lactococcus lactis*.

4. (Cancelled).

5. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 1, wherein said (*thyA*) mutant is further transformed with a transforming plasmid,

wherein said transforming plasmid does not encode an active thymidylate synthase.

6. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 5, ~~further comprising a gene encoding a molecule of interest~~ wherein the transforming plasmid comprises the gene encoding a heterologous prophylactic or therapeutic molecule.

7. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of ~~claim 5~~ any one of claims 1, 2, 5, or 6, wherein ~~said molecule of interest is the gene encoding a heterologous prophylactic or therapeutic molecule encodes~~ Interleukin-10.

8.-9. (Cancelled).

10. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of ~~claim 9~~ any one of claims 1, 2, 5, or 6, wherein ~~the molecule of interest is gene encoding a heterologous prophylactic or therapeutic molecule encodes~~ Interleukin-10 and wherein the *Lactococcus* species is *Lactococcus lactis*.

11. (Withdrawn and Currently Amended) A method for delivering a ~~molecule of interest~~ heterologous prophylactic or therapeutic molecule to a subject, said method comprising administering the transformed strain of *Lactococcus* species of ~~claim 6~~ any of claims 1, 21, 32, and 67 to the subject.

12. (Currently Amended) A composition comprising:
the isolated thymidylate synthase (*thyA*) mutant of ~~claim 5~~ claim 1.
13. (Currently Amended) The composition of ~~claim 12~~ claim 65, ~~wherein the isolated thymidylate synthase (*thyA*) mutant further comprises a gene encoding a molecule of interest~~ wherein the transforming plasmid comprises the gene encoding a heterologous prophylactic or therapeutic molecule.
14. (Currently Amended) The composition of ~~claim 13~~ any of claims 12, 15, or 65, wherein ~~said molecule of interest is~~ the gene encoding a heterologous prophylactic or therapeutic molecule encodes Interleukin-10.
15. (Currently Amended) The composition of ~~claim 12~~ any of claims 12, 13, or 65, wherein said *Lactococcus* species is *Lactococcus lactis*.
16. (Cancelled).
17. (Currently Amended) The composition of ~~claim 16~~ any of claims 12, 13, or 65, wherein ~~the molecule of interest is~~ the gene encoding a heterologous prophylactic or therapeutic molecule encodes Interleukin-10 and wherein said *Lactococcus* species is *Lactococcus lactis*.
18. (Withdrawn and Currently Amended) A method of treating inflammatory bowel disease in a subject, said method comprising:
administering to the subject a transformed strain of *Lactococcus* species of ~~claim 6~~ any of claims 1, 21, 32, and 67.
19. (Withdrawn and Currently Amended) The method of claim 18, wherein ~~the molecule of interest is~~ the gene encoding a heterologous prophylactic or therapeutic molecule encodes Interleukin-10.

20. (Cancelled).

21. (Currently amended) An isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* ~~bacterium~~ species, said *thyA* mutant comprising:

~~a strain of *Lactococcus* bacterium; and~~

~~a means for encoding an inactive *Lactococcus* thymidylate synthase gene and a gene encoding a heterologous prophylactic or therapeutic molecule wherein said means for encoding an inactive *Lactococcus* thymidylate synthase is incorporated into the genome of said strain of *Lactococcus* bacterium.~~

22. (Currently Amended) An isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* ~~bacterium~~ species, said *thyA* mutant comprising:

~~a strain of *Lactococcus* bacterium; and~~

~~a means for encoding an inactive *Lactococcus* thymidylate synthase wherein said means for encoding an inactive *Lactococcus* thymidylate synthase is incorporated into the genome of said strain of *Lactococcus* bacterium; and~~

a gene encoding a heterologous prophylactic or therapeutic molecule;

wherein said strain of *Lactococcus* ~~bacterium~~ species comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5.

23. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of ~~claim 24~~ any of claims 21, 24, or 25, wherein the *Lactococcus* bacterium is a *Lactococcus lactis* bacterium.

24. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of claim 21, further comprising a transforming plasmid; and

wherein said transforming plasmid does not encode an active thymidylate synthase.

25. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of claim 24, ~~further comprising a gene encoding a molecule of interest~~ wherein the transforming plasmid comprises the gene encoding a heterologous prophylactic or therapeutic molecule.

26. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of ~~claim 25~~ any of claims 21, 24, or 25, wherein said molecule of interest is the gene encoding a heterologous prophylactic or therapeutic molecule encodes Interleukin-10.

27.-28. (Cancelled).

29. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of ~~claim 28~~ any of claims 21, 24, or 25, wherein the molecule of interest is the gene encoding a heterologous prophylactic or therapeutic molecule encodes Interleukin-10 and wherein the *Lactococcus* species is *Lactococcus lactis*.

30. (Previously Presented) A composition comprising: the isolated thymidylate synthase (*thyA*) mutant of claim 21.

31. (Currently Amended) The isolated *thyA* mutant of a strain of *Lactococcus* species of claim 1, wherein said ~~nucleic acid encoding~~ strain of *Lactococcus* species comprises an inactive active *Lactococcus* thymidylate synthase comprises comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5.

32. (Currently Amended) An isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species, wherein said *thyA* mutant comprises a ~~nucleic acid encoding~~ an inactive *Lactococcus* thymidylate synthase gene and a gene encoding a heterologous prophylactic or therapeutic molecule, and wherein said *thyA* mutant produced by a process comprising:

providing a strain of *Lactococcus* species comprising a thymidylate synthase gene comprising

at least 100 contiguous nucleotides that are at least 90% identical to ~~a region of~~
SEQ ID NO: 1; and

at least 100 contiguous nucleotides that are at least 90% identical to ~~a region of~~
SEQ ID NO:2; and

altering said *Lactococcus* thymidylate synthase gene to inactivate the thymidylate synthase encoded thereby, wherein the gene encoding said heterologous prophylactic or therapeutic molecule is integrated within, or replaces a part of or the entire thymidylate synthase gene.

33. (Previously Presented) The isolated *thyA* mutant of a strain of *Lactococcus* species according to claim 32, wherein said *Lactococcus* thymidylate synthase gene comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 5.

34. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 32, wherein altering said *Lactococcus* thymidylate synthase gene to inactivate the *Lactococcus* thymidylate synthase encoded thereby comprises gene disruption.

35. (Previously Presented) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to ~~claim 32~~ any of claims 32, 34, 37 or 38, wherein the *Lactococcus* species is *Lactococcus lactis*.

36. (Cancelled).

37. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 32, wherein said (*thyA*) mutant is transformed with a transforming plasmid,

wherein said transforming plasmid does not encode an active thymidylate synthase gene.

38. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to claim 37, ~~further comprising a gene encoding a molecule of interest~~ wherein the transforming plasmid comprises the gene encoding a heterologous prophylactic or therapeutic molecule.

39. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to ~~claim 37~~ any of claims 32, 34, 37, or 38, wherein the molecule of interest is the gene encoding a heterologous prophylactic or therapeutic molecule encodes Interleukin-10.

40.-41. (Cancelled).

42. (Currently Amended) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species according to ~~claim 41~~ any of claims 32, 34, 37, or 38, wherein the molecule of interest is the gene encoding a heterologous prophylactic or therapeutic molecule encodes Interleukin-10 and wherein the *Lactococcus* species is *Lactococcus lactis*.

43. through 64. (Cancelled).

65. (New) The composition of claim 12, wherein said (*thyA*) mutant is further transformed with a transforming plasmid,
wherein said transforming plasmid does not encode an active thymidylate synthase.

66. (New) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of claim 21, wherein the gene encoding a heterologous prophylactic or therapeutic molecule is integrated within, or replaces a part of or the entire thymidylate synthase gene of said strain of *Lactococcus* species.

67. (New) An isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species, said *thyA* mutant comprising:

an inactive *Lactococcus* thymidylate synthase gene and a gene encoding a heterologous prophylactic or therapeutic molecule; and

wherein said *thyA* mutant is produced by a process comprising:

providing a strain of *Lactococcus* species comprising a *Lactococcus* thymidylate synthase gene; and

altering said *Lactococcus* thymidylate synthase gene to inactivate the thymidylate synthase encoded thereby, wherein the gene encoding said heterologous prophylactic or therapeutic molecule is intergreted within or replaces a part of or the entire thymidylate synthase gene.

68. (New) The isolated thymidylate synthase (*thyA*) mutant of a strain of *Lactococcus* species of any one of claims 1, 2, 5, 6, 12, 13, 21, 22, 24, 25, 30-34, 37, 38, 65, or 66, wherein said strain of *Lactococcus* species is MG1363.